

BOOK REVIEW

Lupus. Molecular and Cellular Pathogenesis. Edited by Gary M. Kammer and George C. Tsokos. Umana Press, Totowa, NJ, 1999 (708 pp). Lupus is an enigmatic disease that may correctly be identified as the sum of various diseases with different pathogenic mechanisms and different clinical expressions. Often it puzzles expert clinicians and the treatment of individual patients may challenge established protocols. Lupus is the prototypic systemic "autoimmune" disease that has challenged a number of theories formulated in order to understand the rules governing the immune system. Indeed, by accommodating new findings related to lupus pathogenesis into the general immune mainframe we have shaped our vision of the immune system. Unveiling the various aspects of lupus pathogenesis will substantially improve our knowledge of the immune system physiology. No wonder that an enormous research effort is currently being devoted to unravelling the secrets of such a disease. In this book the authors have attempted to convey different areas of this research in a single book and keep it palatable to readers with heterogeneous interests. Topics as varied as molecular genetics, cellular immunology, biochemical analysis of perturbed intracellular signals, antibody production, relationship between infectious agents and deviated or blunted immune response, generation of antigenic determinants derived from genuine self proteins (components), inflammatory stimuli secondary to immune-complex formation, complement and complement receptors, murine models of the disease, new approaches to treatment, to mention but a few, are covered with up-to-date reviews in the 40 chapters composing the book edited by Kammer and Tsokos.

Not being directly involved in lupus research, I thought that altered T helper cells were unavoidable players in SLE pathogenesis and were leading to B cell anarchic autoantibody production. This is not the case. I learnt in this book that also mice lacking CD4⁺ T cells can produce high titers of IgG autoantibodies. This is just to mention one of the numerous misconceptions that this reader had and was forced to correct while avidly reading this book. In the preface the editors anticipate this possibility and are well aware of the breadth and depth of their book.

Significantly, across the various topics there are dominant recurring themes. One of these is related to cytokines. In no less than 10 chapters cytokines are extensively treated: cytokine genes, cytokine knock outs, T helper cell and cytokines, regulatory T cell subsets and cytokines, inflammatory cytokines, B cell and cytokines. Lupus and murine lupus models characteristically challenge simplification and schematization. For instance, in front of lupus the paradigmatic classification in type I and type II immune responses falls apart. By comparing the data reported on cytokines and the interpretation provided by contributors deeply involved in the field, the reader is enormously enriched. He is put in the position of being able to critically appreciate subtle differences that make up the beauty of nature and of its perverted states and go well beyond easy messages. Another theme running through several chapters is apoptosis. The elegant approach offered by A. Rosen and L. Casciola-Rosen to understand how apoptosis may provide the conditions for the generation of autoantibodies to nucleoproteins is one of the most fascinating contributions of this book. DNA, DNA methylation, DNA antibodies and their relationship to renal pathology are obviously treated in depth. It is important also to mention that costimulatory molecules are also discussed in-depth

with major emphasis on B7.1, B7.2 and their ligands CD28 and CTLA-4, as well as on CD40 and CD40 ligands. We are told that both couples of ligand-receptor pairs qualify for possible targeting in human disease in the light of promising results observed in murine lupus and of the documented alterations of CD40 ligand expression in human T cells, B cells, and endothelial cells.

It is often questionable whether books covering specific aspects of the advancement in science and medicine are worthwhile reading. In this particular case the chapters dealing with the immunopathogenesis of lupus have to compete on the one hand with some well-established and regularly updated behemoth textbooks such as the Dubois' *Lupus Erythematosus* (ed. D.J. Wallace, B.H. Hahn, 5th edn, 1997) or the *Systemic Lupus Erythematosus* (ed. R.G. Lahita, 3rd edn, 1999), and on the other hand with punctual reviews published by slim, highly flexible, up-front periodicals specializing in reviewing scientific advancement. Kammer and Tsokos have succeeded, I believe, in focusing the attention of the 86 contributing authors on to some simple points, with the result that their book easily stands on its own beside the above-mentioned alternatives. Firstly, the references quoted in the various chapters are well poised, with a mix of historical ones and very recent ones. Secondly, the authors were asked to keep in mind four issues while writing: their working hypothesis, the relationship between the hypothesis and the advancement of understanding of lupus pathogenesis, how novel information allows new insights in the field and where to direct research in the next 5 years. By sticking to this request the contributors have produced a book that, notwithstanding the heterogeneity of the topics, has a high degree of homogeneity in its own right. The reader thus can easily jump from chapter to chapter without losing his way, meanwhile enjoying the enthusiasm of researchers promoting the rationale standing behind the efforts of their laboratories. Indeed, this book is a window to the future.

Reviewers are pushed to find errors, mistakes and imperfections. What about this book? It is a shame that all authors selected by the editors with the exception of a single contributor (J.A. Schifferli) are working in the United States. Does this mean that no viable research on lupus is performed outside the USA? This is not the case, I believe. Suffice to mention that many references quoted in the book are from authors working in countries other than the USA. Thus, the choice to stick with people working in a familiar milieu may reflect a regrettable tendency to disregard new information coming from outside, unless, of course, authors from abroad declined to contribute to the book for symmetrical reasons.

In conclusion, I strongly recommend reading this book. It has the major merit of presenting in a coordinated fashion many new findings on a disease that remains largely mysterious. This book has the potential to encourage cross-fertilization among researchers interested in the field of autoimmunity, and provides a valuable tool for newcomers to get a sense of the daunting problems that remain to be solved in order to better understand the regulation and dysregulation of the immune system.

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